

Galactosemia Variations

August 2007

This information sheet will summarize the genetics of galactosemia and explain some of the issues involved when your child is identified as having a galactosemia allele variant.

DEFINITIONS

Allele: Alternative form of a gene that occupies the identical site on the chromosome and determines alternative characters in the inheritance. May also be called a variant gene.

Autosomal recessive disorder: A condition in which two abnormal genes need to be present in order for the disease to exist.

Carrier: A condition in which there is one normal gene and one abnormal gene present. The normal gene supplies the necessary "instruction" for the body to operate.

WHAT IS GALACTOSEMIA?

Galactosemia is an autosomal recessive disorder in which galactose accumulates in the blood, tissues, and organs of the body. The State of Utah tests for the galactose-1-phosphate uridylyltransferase (GALT) enzyme deficiency. In this condition the body lacks the enzyme to break down the sugar galactose. Galactose is found primarily in milk and milk products (the milk sugar lactose breaks down into galactose and then glucose) and in some fruits and vegetables. Untreated, individuals with galactosemia may have symptoms such as vomiting, jaundice, enlarged liver, cataracts, and septicemia. If not treated, it may affect your child's development.

To prevent problems, a special diet that is galactose free is recommended. This would include a milk-free formula, such as Prosobee or Isomil, and a list of recommended foods.

The two most commonly treated types of galactosemia are classic galactosemia and Duarte galactosemia.

A person with classic galactosemia has two galactosemia genes (gg) and needs to be on a lifelong galactose restricted diet. There is **NO** GALT enzyme made to digest galactose. He or she is at risk to have medical and developmental complications.

A person with Duarte galactosemia has one Duarte allele and one galactosemia gene (Dg). The Duarte gene makes a reduced amount of the needed GALT enzyme. In Utah treatment is recommended for about the first year of life. Most children with Duarte galactosemia develop normally and do not have medical complications. There have been case reports of children with Duarte galactosemia with some of the symptoms of classic galactosemia. After a year of treatment (sometimes a little longer), once the child's diet diversifies and the liver grows, there is no longer a need for continued treatment.

GALT genes come in different forms called variants. Several different variant genes can code (or make) the GALT enzyme. Most variants make less of the enzyme than the N or "normal" gene. One variant actually makes it more efficient than the normal gene.

Each person has a different combination of GALT genes or variants in their unique gene pair, depending on which gene they inherited from each parent. Different combinations of a gene pair result in different levels of GALT enzyme activity in the body.

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The table below describes the genes seen in Utah. The activity level shows the efficiency of the GALT enzyme. Thirteen percent of the population has a Duarte gene.

Gene	Symbol	Activity level
Normal	N	100%
Galactosemia - non-functioning	g	0%
Duarte - partially functioning	D	50%
Los Angeles - above normal functioning gene	LA	125%

This table shows the activity of the GALT enzyme depending on the gene pair.

	Genotype (gene pair)	Diagnosis	GALT enzyme Activity	GALT enzyme function	Clinical Management
2 normal genes	NN	Normal	100%	Normal	None
2 nonfunctioning genes	gg	Classical Galactosemia	0%	Absent	Diet, specialized medical care
2 Duarte genes	DD	Homozygous Duarte Variant	50%	Reduced	None
Combinations:	Ng	Galactosemia Gene Carrier	50%	Reduced	None
	ND	Duarte Variant Carrier	75%	Slightly reduced	None
	Dg	Duarte Galactosemia	5-20%	Greatly reduced	Diet
	NLA	LA Variant Carrier	112%	Above normal	None
	LAG	Galactosemia Gene Carrier	62%	Slightly reduced	None

IS GALACTOSEMIA A GENETIC CONDITION?

Yes, it is genetic. It affects males and females equally and occurs in all races.

WHAT IS A CARRIER OF A GALACTOSEMIA GENE VARIANT?

A person with just one allele/variant galactosemia gene and one normal gene is called a carrier. A carrier does not have galactosemia and will not have any signs or symptoms, however a carrier may pass their gene to their children. He or she has a 50% chance of passing the D allele to his/her child.

WHAT TESTING DO WE RECOMMEND IN FAMILIES WITH A CHILD WHO IS A DN CARRIER?

Parents of a child who is a DN carrier are at somewhat less at risk than the general population to have a child with classic galactosemia and at an increased risk (1 in 800) to have a child with Duarte galactosemia. We can consider genotyping parents for galactosemia alleles to settle the question of whether they are at risk to have a child with Duarte galactosemia, since we treat the condition in Utah. If the parents have a DN genotype and an NN genotype, the parents are not at risk to have a child with Duarte galactosemia. If the parents have a DN genotype and a gN genotype, their risk is 1 in 4 with each pregnancy to have a child with Duarte galactosemia. However, given the mild symptoms, we feel that genotyping is a parental decision.

If the parents do not want genotyping, another option is to genotype future offspring for galactosemia alleles. Although newborn screening will pick up many children with Duarte galactosemia, it has a substantial false negative rate. If the family and their physician would like to test any future offspring, blood can be sent to the Children's Hospital Los Angeles Dept. of Pathology & Laboratory Medicine (323-669-2590) in Los Angeles for genotyping.

If one parent has a DN type and one parent has an NN type, there are no precautions that need to be taken in another pregnancy. If one parent has a DN type and the other a gN type, it is recommended that other children be genotyped at birth to see if they have the Dg type, which we treat in Utah.

For further information or testing, an appointment can be arranged with a genetic counselor by calling 801- 585-2457.